

CLAIMS

1. Use of a polypeptide, or a derivative or analogue thereof, comprising repeats of a peptide derived from a Heparan Sulphate Proteoglycan (HSPG) receptor binding region of an apolipoprotein for the manufacture of a medicament for the treatment of

5 a bacterial infection.

2. Use according to claim 1, wherein the peptide is derived from a Heparan Sulphate Proteoglycan (HSPG) receptor binding region of apolipoprotein B or apolipoprotein E.

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3. Use according to any preceding claim, wherein the peptide is derived from an apolipoprotein B LDL receptor binding domain cluster B, or from an apolipoprotein E LDL receptor binding domain cluster B.

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4. Use according to any preceding claim, wherein the polypeptide comprises at least two RKR motifs.

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5. Use according to any preceding claim, wherein the polypeptide comprises a tandem dimer repeat of: SEQ ID No.1; SEQ ID No.2; SEQ ID No.96; or a derivative thereof wherein at least one amino acid residue, other than RKR motifs, is replaced by an Arginine (R), Tyrosine (Y), Methionine (M), Isoleucine (I), Phenylalanine (F), Tryptophan (W), or a derivative thereof.

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6. Use according to claim 5, wherein the replaced or substituted residue is the first, second, third, seventh, eighth, ninth, tenth, eleventh, twelfth, sixteenth, seventeenth or eighteenth residue of the polypeptide.

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7. Use according to either claim 5 or claim 6, wherein the at least one amino acid substitution is a Phenylalanine (F) residue or a Tryptophan (W) residue, or a derivative thereof.

8. Use according to any preceding claim, wherein the polypeptide has the formula:

$$\{abcRKRxyz\} + \{a'b'c'RKRx'y'z'\} \quad (\text{formula I})$$

wherein

a & a' = is independently selected from Arginine (R); Tyrosine (Y); Methionine (M); Isoleucine (I); Phenylalanine (F); Tryptophan (W); Leucine (L); Lysine (K); Histidine (H); or is deleted;

5 b & b' = is independently selected from Arginine (R); Tyrosine (Y); Methionine (M); Isoleucine (I); Phenylalanine (F); Tryptophan (W); Leucine (L); Lysine (K); or is deleted;

c & c' = is independently selected from Arginine (R); Tyrosine (Y); Methionine (M); Isoleucine (I); Phenylalanine (F); Tryptophan (W); Leucine (L); Lysine (K); Histidine 10 (H); or Threonine (T); or is deleted;

x & x' = is independently selected from Arginine (R); Tyrosine (Y); Methionine (M); Isoleucine (I); Phenylalanine (F); Tryptophan (W); Leucine (L); Lysine (K); Histidine (H); or Glycine (G); or is deleted;

y & y' = is independently selected from Arginine (R); Tyrosine (Y); Methionine (M); 15 Isoleucine (I); Phenylalanine (F); Tryptophan (W); Leucine (L); Lysine (K); Histidine (H); or is deleted;

z & z' = is independently selected from Arginine (R); Tyrosine (Y); Methionine (M); Isoleucine (I); Phenylalanine (F); Tryptophan (W); Leucine (L); Lysine (K); Histidine (H); or is deleted.

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9. Use according to claim 8, wherein the polypeptide comprises at least one additional amino acid, which may be independently selected from Arginine (R); Tyrosine (Y); Methionine (M); Isoleucine (I); Phenylalanine (F); Tryptophan (W); Leucine (L); Lysine (K); Histidine (H), and which additional amino acid is added before the amino acid at position 'a' in the peptide of formula I at the N-terminal.

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10. Use according to any preceding claim, wherein the polypeptide comprises: a repeat of the peptide apoE₁₄₁₋₁₄₉ (SEQ ID NO. 1) or a truncation thereof; or a repeat of a variant of the peptide apoE₁₄₁₋₁₄₉ in which at least one Leucine (L) residue is 30 replaced by Tryptophan (W), Arginine (R), Lysine (K), Tyrosine (Y) or Phenylalanine (F), for the manufacture of a medicament for the treatment of a bacterial infection.

11. Use of a polypeptide comprising: a repeat of the peptide apoE₁₄₁₋₁₄₉ (SEQ ID NO. 1) or a truncation thereof; or a repeat of a variant of peptide apoE₁₄₁₋₁₄₉ in which at least one Leucine (L) residue is replaced by Tryptophan (W), Arginine (R), Lysine (K), Tyrosine (Y) or Phenylalanine (F), for the manufacture of a medicament for the treatment of a bacterial infection.

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12. Use according to claim 11, wherein the polypeptide comprises a repeat of apoE₁₄₁₋₁₄₉ (SEQ ID No.1) or a truncation thereof, characterised in that at least one Leucine (L) residue is replaced by a Tryptophan (W), or a Phenylalanine (F) residue.

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13. Use according to either claim 11 or claim 12, wherein the tandem repeat comprises at least two substitutions independently selected from Tryptophan (W), Arginine (R), Lysine (K), Tyrosine (Y), or Phenylalanine (F) substitutions.

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14. Use according to any preceding claim, wherein the polypeptide comprises the amino acid sequence: LRKLRKRLLLRKLRKRL (SEQ ID NO. 6); WRKWRKRWWRKWRKRW (SEQ ID No. 7); WRKWRKWRKWRKWRK (SEQ ID No. 8); WRKWRKRWWRKLRKRL (SEQ ID No. 9); YRKYRKYYYRKYRKYY (SEQ ID No. 10); LRKLRKRLRKLRK (SEQ ID No. 11); LRKRLRLRKRL (SEQ ID No.3); FRKFRKFFFRRKFRKRFF (SEQ ID No.48); WRKWRKRWWRKWRKRW (SEQ ID NO.63); WRKWRKWRKWRKRW (SEQ ID NO.64); WRKWRKRWWRFRKWRKRW (SEQ ID NO.65); WRKWRKRFWRKWRKRF (SEQ ID NO.66); WRKRWWRWRKRWWR (SEQ ID NO.67); LRKLRKRLRLRKRL (SEQ ID NO.68); WRKWRKRWWRWRKWRKRW (SEQ ID NO.69); LRKLRKRLWRKWRKRW (SEQ ID NO.70); LRKLRKRLRLRKRL (SEQ ID NO.71); LRKLRKRLWRKWRKRL (SEQ ID NO.72); WRKWRKRLRKRL (SEQ ID NO.73); WRKLRKRLRKRL (SEQ ID NO.74); WRKWRKFFFRRKWRKRW (SEQ ID NO.75); or

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WRKWRKRWWRFRKFRKRFF (SEQ ID NO.76).

15. Use according to any one of claim 1 to 9, wherein the polypeptide comprises repeats of a peptide derived from an HSPG receptor binding region of apoB.

16. Use of a polypeptide, or a derivative or analogue thereof, comprising repeats of a peptide derived from an HSPG receptor binding region of apolipoprotein B for the manufacture of a medicament for the treatment of a bacterial infections.

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17. Use according to claim 15 or 16, wherein the polypeptide is derived from an apolipoprotein B LDL receptor binding domain cluster B.

18. Use according to either claim 16 or claim 17, wherein the polypeptide comprises a
10 repeat of apoB₃₃₅₉₋₃₃₆₇ (SEQ ID No. 2) or a truncation or variant thereof.

19. Use according to any one of claims 16 to 18, wherein the polypeptide comprises at least two RKR motifs.

15 20. Use according to any one of claims 16 to 19, wherein the polypeptide has the sequence of RLTRKRGGLKRLTRKRGGLK (SEQ ID No.12) or a truncation thereof wherein at least one amino acid residue, other than the RKR motifs, has been replaced by a Glycine (G), Threonine (T), Histidine (H), Tryptophan (W), Arginine (R) or Leucine (L) residue or derivatives thereof.

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21. Use according to claim 20, wherein the at least one amino acid residue has been replaced by a Tryptophan (W), Arginine (R) or Leucine (L) residue or derivative thereof.

25 22. Use according to any one of claims 16 to 21, wherein the polypeptide has formula:
 $\{abcRKRxyz\} + \{a'b'c'RKRx'y'z'\}$ (formula IV)

wherein

a & a' = is independently selected from a positively charged residue, which may be selected from either Arginine (R) or Lysine (K) or Histidine (H); Leucine (L);

30 Tryptophan (W); or is deleted;

b & b' = is independently selected from Leucine (L); Arginine (R); Lysine (K); or is deleted;

c & c' = is independently selected from Threonine (T); Tryptophan (W); or a positively charged residue, which may be selected from Arginine (R) or Lysine (K) or Histidine (H);

x & x' = is independently selected from Glycine (G); Tryptophan (W); Leucine (L);

5 or a positively charged residue, which may be selected from Arginine (R) or Lysine (K) or Histidine (H);

y & y' = is independently selected from Leucine (L); a positively charged residue, which may be selected from Arginine (R) or Lysine (K) or Histidine (H); or is deleted;

10 z & z' = is independently selected from a positively charged residue, which may be selected from Arginine (R) or Lysine (K) or Histidine (H); or Leucine; or is deleted.

23. Use according to any one of claims 16 to 22, wherein the polypeptide is:

RTRKRGRRTRKRGR (SEQ ID No.13); LRKRKRLLRKRKRL (SEQ ID No.14);

15 LRKRKRLRKLKRKRLRK (SEQ ID No.15); WRWRKRWRKWRWRKWRKWRK (SEQ ID No.16); LLRKRLKRLLRKRLKRL (SEQ ID NO.80); RRWRKRWRKWRWRKWRK (SEQ ID NO.83);

KRWRKRWRKWRWRKWRK (SEQ ID No.84); LRWRKRWRKWRWRKWRKWRK (SEQ ID No.85); HRWRKRWRKWRWRKWRK (SEQ ID No.86);

20 RWRKRWRKWRWRKWRK (SEQ ID NO.87); RRWRKRWRKRRWRKWRK (SEQ ID NO.88); LRWRKRWRKLRWRKWRK (SEQ ID No.89); HRWRKRWRKHRWRKWRK (SEQ ID No.90); RWRKRWRKWRKWRKWRK (SEQ ID NO.91); RWRKRGGRKWRKRGGRK (SEQ ID No.92); RWRKRWRKWRKWRK (SEQ ID No.93); RKRGWKWRKRGWKW (SEQ ID No.94); or RLTRKRGRLTRKRG (SEQ ID No.95).

24. Use according to any one of claims 16 to 19, wherein the polypeptide has the sequence of RLTRKRGRLKRLTRKRG (SEQ ID No.12).

30 25. A polypeptide comprising a repeat of the peptide apoE₁₄₁₋₁₄₉ (SEQ ID No.1) or a truncation thereof, characterised in that at least one Leucine (L) residue is replaced by Tyrosine (Y) or Phenylalanine (F).

26. A polypeptide, derivative or analogue thereof, comprising an amino acid sequence of: SEQ ID No.3 (GIN 2); SEQ ID No.4 (GIN 11); SEQ ID No. 67 (MU 81); SEQ ID No. 68 (MU 82); SEQ ID No. 80 (MU 24); SEQ ID No. 94 (MU 73) or SEQ ID No. 95 (MU 74).

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27. Polypeptides according to claim 25 or 26 for use as medicaments.

28. Use of polypeptides according to claim 27, for the manufacture of medicament for the treatment of a bacterial infection.

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29. Use of polypeptides according to any preceding claim for treating *Staphylococcus*, *Pseudomonadales* or *Streptococci* infections.

30. A nucleic acid sequence encoding a polypeptide according to any preceding claim.

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31. A method of preventing and/or treating a bacterial contamination comprising coating an object or a surface in need thereof with an amount of a polypeptide according to any preceding claim that is effective for killing or preventing growth of bacteria.

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32. A method according to claim 31 wherein an object is coated and is selected from: medical devices, lenses, contact lenses, catheters, stents, wound healing dressings, contraceptives, surgical implants and replacement joints.

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33. A method according to claim 31 wherein a surface is coated and the surface is selected from: hospital ward surfaces, operating theatre surfaces, kitchen surfaces and sanitary surfaces.

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34. A contact lens at least partially coated with a peptide, derivative or analogue thereof, according to any preceding claim.